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BUCKET NO.: ISIS-5325

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Charles Allerson, et al.

Confirmation No.: 5641

Application No.: 10/701,007

Group Art Unit: 1645

Filing Date: November 4, 2003

Examiner: Not Yet Assigned

**For: COMPOSITIONS COMPRISING ALTERNATING 2'-MODIFIED
NUCLEOSIDES FOR USE IN GENE MODULATIONS**

EXPRESS MAIL LABEL NO: EL998519145US

DATE OF DEPOSIT: September 14, 2004

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

- ☒ In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in § 1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or

before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

- ☐ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.116 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

- ☐ Certification in Accordance with § 1.97(e) is attached; or
- ☐ The fee of **\$180.00** as set forth in § 1.17(p) is attached.

- ☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of **\$180.00** as set forth in § 1.17(p).

- ☒ Copies of reference numbers 104 - 111 listed on the attached Form PTO-1449 are enclosed herewith.

- ☒ A copy of reference number 112 on the attached Form PTO 1449 is not required to be submitted pursuant to 37 CFR § 1.98(a)(2)(i).

- ☐ Copies of references - are not being submitted because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application number , filed for which a claim for priority under 35 U.S.C. § 120 has been made in the instant application.

- ☐ The relevance of those listed references which are not in the English language is as follows:

DOCKET NO.: ISIS-5325

- 3 -

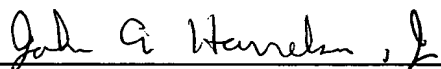
PATENT

Enclosed is a copy of the PCT International Search Report dated August 23, 2004
(number 104 on Form PTO-1449), which indicates the references considered to be relevant.

There are no listed references which are not in the English language.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-
3050. This form is submitted in duplicate.

Date: September 14, 2004



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| Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office | | Docket No. ISIS-5325 | Application No. 10/701,007 |
| | | Applicant Charles Allerson, et al. | |
| | | Filing Date November 4, 2003 | Group 1645 |
| | | Confirmation No. 5641 | |
| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) | | | |
| | 104 | Copy of the PCT International Search Report dated August 23, 2004 (PCT/US03/35063) | |
| | 105 | Beigelman, L., et al., "Chemical modification of hammerhead ribozymes," <i>J. of Biological Chem.</i> , 1995 , 270(43), 257082-25708 | |
| | 106 | Caplen, N.J., et al., "Specific inhibition of gene expression by small double-stranded RNAs in invertebrate and vertebrate systems," <i>PNAS</i> , 2001 , 98(17), 9742-9747 | |
| | 107 | Czauderna, F., et al., "Structural variations and stabilizing modifications of synthetic siRNAs in mammalian cells," <i>Nucleic Acids Res.</i> , 2003 , 31(11), 2705-2716 | |
| | 108 | Elbashir S.M., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," <i>Nature</i> , 2001 , 411, 494-498 | |
| | 109 | Paddison, P.J., et al., "Stable suppression of gene expression by RNAi in mammalian cells," <i>PNAS</i> , 2002 , 99(3), 1443-1448 | |
| | 110 | Sui, G., et al., "A DNA vector-based RNAi technology to suppress gene expression in mammalian cells," <i>PNAS</i> , 2002 , 99(8), 5515-5520 | |
| | 111 | Yu, J.-Y., et al., "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells," <i>PNAS</i> , 2002 , 99(9), 6047-6052 | |
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| EXAMINER | | DATE CONSIDERED | |

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| Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office | Docket No. ISIS-5325 | Application No. 10/701,007 |
| | Applicant Charles Allerson, et al. | |
| | Filing Date November 4, 2003 | Group 1645 |
| | Confirmation No. 5641 | |

U. S. PATENT DOCUMENTS

| Examiner Initial | | Document No. | Date | Name | Class | Subclass |
|------------------|-----|-----------------|----------|------------------|-------|----------|
| | 112 | 2003/0143732 A1 | 07/31/03 | Fosnaugh, et al. | 435 | 325 |
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FOREIGN PATENT DOCUMENTS

| Examiner Initial | | Document No. | Date | Country | Translation | |
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